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AGE-RELATED AMPLITUDE CHANGES OF THE PATTERN REVERSAL EVOKED POTENTIAL DEPEND ON STIMULUS SPATIAL FREQUENCY AND CONTRAST

KARL F. VAN ORDEN[1] and JOSEPH F. STURR[2]

[1]Environmental Medicine Department, Naval Medical Research Institute, Bethesda, MD 20814-5055 and
[2]Department of Psychology, Syracuse University, Syracuse, NY 13244-2340, U.S.A.

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Summary—1. Previous studies which have shown that the amplitude of the P1 component of the pattern reversal evoked potential (PREP) is not affected by age may have utilized stimulus configurations which prevented detection of age-related differences. The present study investigated PREP amplitudes in young and older subjects with stimulus and analysis parameters designed to specifically examine N1 and P1 amplitudes in 10 young and 10 elderly males (mean ages 20 and 64.5 yr).

2. Since a recent report suggests that N1 and P1 PREP components may reflect cortical activity resulting from the input of distinct visual pathways of the lateral geniculate nucleus, subjects viewed sinusoidal grating stimuli of 0.6 and 6 c/deg which phase-reversed every 265 ms. Stimulus contrasts were set at 50% or 6% above threshold contrast.

3. Significantly smaller P1 amplitudes for 6 c/deg stimulation were found in the elderly for low but not high contrast levels, and older observers had significantly attenuated N1 amplitudes for the 6 c/deg-high contrast stimulus.

4. The age-related changes in N1 and P1 amplitudes were limited to the high stimulus spatial frequency, and thus the results do not support a change specific to either magno or parvocellular LGN mechanisms. The results are discussed within the context of recent research on suprathreshold contrast perception.

Key words—Aging; vision; evoked potentials; contrast; spatial frequency.

INTRODUCTION

A number of studies have been conducted in an attempt to understand changes in the pattern reversal evoked potential (PREP) that occur with age. Because of the clinical utility of the PREP, most experiments have focused on establishing group norms with healthy subjects of varying ages, using high contrast checkerboard patterns. The major positive component of the PREP, the P1, has been most actively studied. Most investigators agree that the latency of the P1 remains unchanged from the late teens into the late fifties and then increases significantly thereafter (Allison *et al.*, 1983; Celesia and Daly, 1977; Shaw and Cant, 1980; Shaw, 1984; Stockard *et al.*, 1979). In addition, the effect of age on P1 latency is more pronounced with smaller patterns (Sokol *et al.*, 1981), and under conditions of lower luminance (Shaw and Cant, 1980). Studies investigating age-related changes in amplitude of the P1 component of the PREP have generally found no significant changes in amplitude over the lifespan (Allison *et al.*, 1984; Celesia *et al.*, 1987; La March *et al.*, 1986; Synder *et al.*, 1981). However, all of the aforementioned studies utilized high contrast checkerboard stimuli, which are known to emit higher spatial harmonic frequencies, stimulate numerous visual mechanisms, and affect the PREP in a complex manner compared to sinusoidal grating stimuli (Bobak, 1989). Previc (1988) points out that one of the major drawbacks of the clinical use of checkerboards for PREP recordings has been the failure to isolate and understand specific PREP components. Alternatively, sinusoidal gratings, which are used by visual psychophysicists, would be more effective stimuli because they would enable the isolation of individual PREP components. For example, Previc (1988) has recorded PREPs with phase reversing sinusoidal stimuli of high and low contrast levels and different spatial frequencies, and he has shown that the primary negative (N1) component is elicited primarily by high contrast-high spatial frequencies, while the P1 component is produced at lower contrast levels, and saturates at higher stimulus

contrasts. It is thus possible that utilizing stimuli of lower contrast levels and specific spatial frequencies might reveal age-related changes in N1 and P1 PREP component amplitudes which heretofore could not be detected with high contrast checkerboard patterns. This issue may be important if the N1 and P1 PREP components arise from distinct neural mechanisms and are perhaps affected differently by aging.

Recent research by Previc suggests that PREP N1 and P1 components may represent the cortical activity arising from the parvo and magnocellular neurons, respectively, of the lateral geniculate nucleus (LGN). Parvocellular units respond optimally to high spatial, low temporal, high contrast stimuli, while magnocellular neurons respond best to low spatial, high temporal low contrast stimulation (Dreher *et al.*, 1976; Kaplan and Shapley, 1982, 1986). Previc observed that N1 and P1 components have amplitude response characteristics, in terms of spatial frequency tuning and contrast saturation, resembling those of parvo and magnocellular neurons.

The purpose of the present study, therefore, was to examine N1 and P1 PREP component amplitude changes with age using sinusoidal grating stimuli. Since Previc's research has tentatively linked the PREP components to their respective neural pathways, N1 and P1 component amplitudes were determined for stimuli of low and high spatial frequencies under low and high stimulus contrast levels. In addition, steps were taken to ensure that age-related ocular changes would not confound the PREP amplitude measures.

METHODS

Subjects

Young (ages 17–26 yr, mean = 20) and older (ages 60–76 yr, mean = 64.5) age groups were composed of 10 male observers each. The young observers were screened on the basis of admitted good ocular and general health. Observers within the older-age-group were recruited from local senior citizen activity centers. They were questioned about their medical histories, and specific information regarding best corrected acuities, lens prescriptions, the incidence of glaucoma, cataracts, drusen and other ocular pathologies was obtained from them and from their eye care practitioners. All older observers had received an eye examination within 10 months of testing. Three of the older observers had a slight cataract in one eye, and one other observer had mild drusen in one eye. None of these conditions was regarded as severe enough for disqualification from the study. Older observers had corrected visual acuities of between 20/20 and 20/25 (average 20/22), while all younger observers reported acuities of 20/20. Males were used exclusively in this experiment in order to avoid variance from well established differences in VEP amplitudes and latencies between males and females (see Celesia *et al.*, 1987; La March *et al.*, 1986). All observers were paid for their participation in the study.

Apparatus

Sinusoidal grating patterns of 0.6 and 6 c/deg were generated on a c.r.t. (60 Hz noninterlaced, P2 phosphor) by a Nicolet CS 2000 contrast sensitivity measurement apparatus and were counterphase flickered at a rate of 1.9 Hz (contrast phase reversed every 264 ms). The screen subtended a visual angle of 9.7(h) × 7.5(w) deg. The mean luminance of the screen was approx. 75 cd/m^2. A 0.5 log unit neutral density filter was placed over the monitor screen for the younger observers, therefore reducing the screen luminance to 25 cd/m^2. The filter was utilized in order to approximately equate old and young observers for optical transmission losses found in older individuals (Owsley *et al.*, 1983). Viewing was binocular throughout the study, and the testing room remained dimly lit (0.4 cd/m^2).

The CS 2000 provided synchronization signals, emitted at each pattern reversal, to start the recording sweep of the signal averager. All evoked potentials were recorded by a Nicolet 1A97 EEG machine and averaged on-line by a Nicolet Pathfinder II signal averaging system. Low and high filter bandpass settings were 1.5 and 60 Hz respectively. Automatic artifact rejection was plus/minus 42.5 μV, and the sweep sample time was 250 ms.

Procedure

Electrode caps (Electro-Cap International Inc. Dallas) were fit to each observer and provided recording electrodes at O_z, O_1 and O_2, points defined anatomically by the International 10–20 System. Electrode impedances were maintained below 10 kΩ. The subject sat 1.7 m from the c.r.t. screen. Some vision researchers have utilized corrective lenses to equate young and

older observers because of the inability of older individuals to accommodate appropriately, particularly for viewing distances of 1 m or less (Owsley *et al.*, 1983; Sturr *et al.*, 1988). The viewing distance of 1.7 m utilized in this study would require a lens of only 0.58 D. While this technique is important for close viewing distances, it was not employed in the present study since the correction would be minor, the highest spatial frequency used was 6 c/deg, and the corrective technique assumes that older observers have a total loss of accommodative power. Additionally, pupil diameter was not measured in these subjects: Sloane *et al.* (1988) have shown that pupil size has little effect on contrast sensitivity in older observers.

In order to set the low contrast levels to some absolute value above contrast threshold for each observer, the contrast thresholds of the stimuli were measured by the method of increasing contrasts. This method has proven to be a reliable procedure for threshold determination in terms of repeatability, speed, and low variance (Ginsburg and Cannon, 1983). At the beginning of a trial, contrast was well below threshold and increased at a slow rate (0–50% in 60 s). When the observer first detected the stimulus, he pushed a button on the response box which signalled the computer to record that contrast. This procedure was repeated three times per stimulus. Three practice trials were included prior to the threshold measures. The order of the stimuli was randomized between subjects.

For each observer, contrast thresholds for the 0.6 and 6 c/deg gratings were used to set the suprathreshold contrast levels for the evoked potential measurements. Suprathreshold contrasts for the low contrast stimuli were set at 6% above absolute threshold, to the nearest percent. For gratings of 0.6 and 6 c/deg flickered at 1.9 Hz, this procedure typically yields suprathreshold contrasts between 7 and 8% respectively. These low contrast levels were chosen because they are clearly visible, yet low enough to predominantly stimulate magnocellular visual mechanisms (Kaplan and Shapley, 1986; Previc, 1988). The high contrast stimuli were set at a level of 50% for all observers since even a 1% difference in contrast is negligible at this level. At least 100 artifact free sweeps were recorded for each of the four stimulus conditions. The measurement of thresholds and evoked potentials described above took approx. 25 min per subject.

RESULTS

Contrast thresholds

Contrast thresholds, used to establish the stimulus contrasts for the VEP recordings, were analyzed by an age group × stimulus spatial frequency (6 and 0.6 c/deg) split-plot ANOVA. As expected, this procedure yielded a significant main effect of Spatial frequency [$F(1, 18) = 94.56$, $P < 0.0005$]. Age was not significant either alone or in combination with spatial frequency.

Visual evoked potentials

For each observer, the records at the O_1, O_2, and O_z recording sites were averaged together to form one waveform for each stimulus condition (0.6 and 6 c/deg at low and high contrasts). This procedure ensured good, relatively noise-free waveforms, particularly at low contrasts. Figure 1 displays typical evoked response from a young and older observer with the N1 and P1 components labeled. N1 and P1 amplitudes were calculated relative to a 25 ms baseline at the onset of the sweep. For consistency, in stimulus conditions which elicited negligible N1 responses, the most negative point between 45 and 110 ms denoted N1.

Separate split plot ANOVAs were run on the N1 and P1 amplitude data. Summary tables are shown in Table 1. The significant triple interaction between age group, contrast, level, and stimlus spatial frequency for N1 amplitudes is shown in Fig. 2, which plots N1 amplitude as a function of stimulus condition for the young and older observers. Compared to the older observers, the young observers displayed significantly larger N1 responses to high contrast 6 c/deg stimulation ($P < 0.001$).

The significant age group by stimulus spatial frequency interaction for P1 amplitudes, as shown in Fig. 3, signals that across levels of contrast, the P1 responses elicited by the 6 c/deg stimulus are significantly greater in the younger observers. However, specific tests of mean differences at low and high contrast levels using the three way interaction error term (from Table 1) and a 0.025 simultaneous error rate revealed that young and older observers differed only for the low contrast P1 response for 6 c/deg stimulation ($P = 0.017$). The differences in P1 amplitude means for the high contrast 6 c/deg condition was not statistically significant ($P = 0.14$) as a function of age.

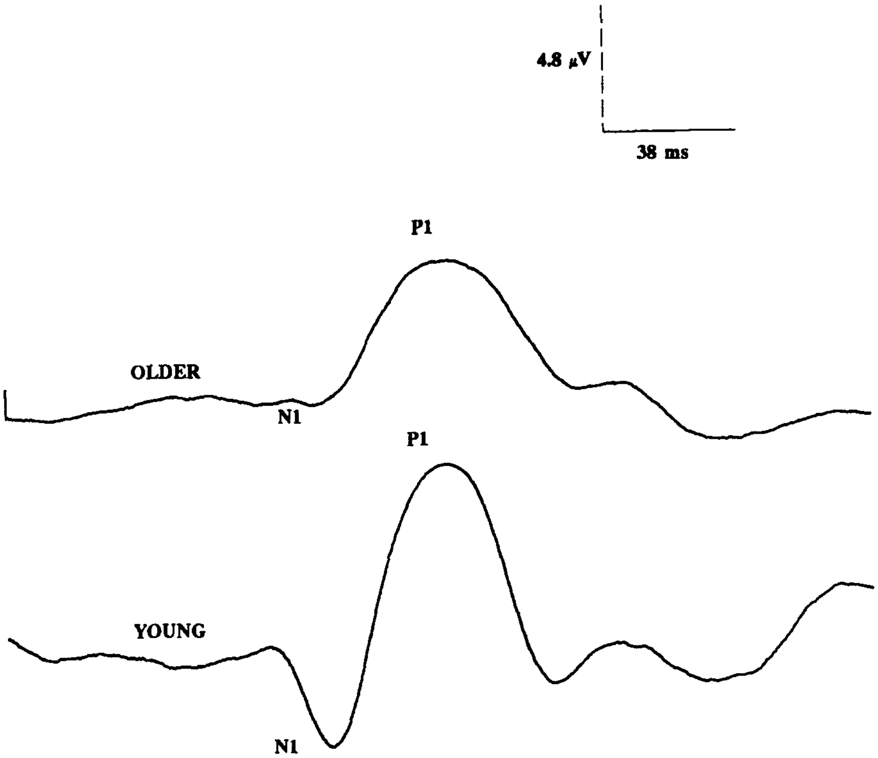

Fig. 1. Typical pattern reversal evoked potentials from a young and an older observer. N1 and P1 components are labeled. Positivity is up.

Table 1. Split plot analysis of variance summary tables for the N1 and P1 amplitude data analyses

Variables	Amplitude analysis Sums of squares	Degrees of freedom	*F*-values
	N1 amplitudes		
Age	15.03	1	3.42
Error	79.10	18	
Contrast	3.75	1	1.16
Age × contrast	17.48	1	5.39*
Error	58.32	18	
Stimulus	10.80	1	5.78*
Age × stimulus	6.37	1	3.41
Contrast × stimulus	7.12	1	3.81
Age × contrast × stimulus	18.28	1	9.78***
Error	67.23	36	
	P1 amplitudes		
Age	5.24	1	0.23
Error	408.98	18	
Contrast	119.32	1	31.51***
Age × Contrast	0.96	1	0.62
Error	68.16	18	
Stimulus	5.78	1	3.77
Age × stimulus	7.08	1	4.62*
Contrast × stimulus	2.32	1	1.51
Age × contrast × stimulus	0.07	1	0.05
Error	55.13	36	

Significance levels: $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.005$.

DISCUSSION

The results of the present study reveal complex age-related changes in PREP N1 and P1 components. Compared to the elderly, young observers demonstrated significantly larger P1 amplitudes for the 6 c/deg stimulus at low but not at high contrast levels. These latter results support previous research showing no significant age-related changes in P1 amplitudes under high contrast viewing conditions (Allison *et al.*, 1984; Celesia *et al.*, 1987; La Marche *et al.*, 1986; Snyder *et al.*, 1981). The largest age related change involved the N1 component amplitudes, which were significantly attenuated in the older observers for the 6 c/deg grating at 50% contrast.

In support of Previc's (1988) data, the N1 and P1 responses from the younger observers mirrored amplitude response characteristics of parvo and magnocellular LGN mechanisms respectively. Since the older observers demonstrated attenuated N1 and P1 responses, a selective effect of age upon either parvo or magnocellular mechanisms is not supported. Of interest is the fact that the age related differences in N1 and P1 amplitudes

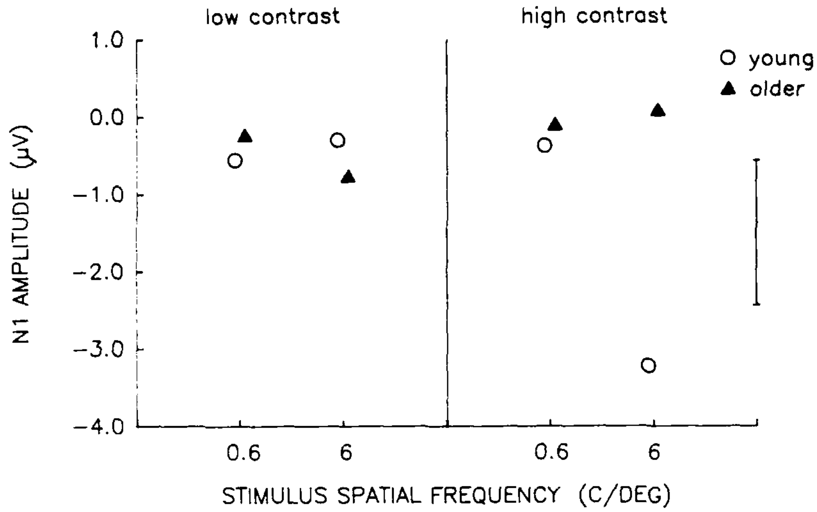

Fig. 2. Mean N1 amplitude in microvolts for young and older subjects (○ and ▲, respectively) plotted as a function of stimulus spatial frequency and stimulus contrast level. Low contrast gratings were set at a level of 6% above threshold contrast for each subject, while high contrast grating were set at 50%. The standard error for the means of young and older observers is shown at the right and is 1.88 μV. Note that greater N1 amplitude is toward the bottom of the figure.

occurred to some extent under conditions in which the N1 and P1 responses have been shown by Previc to be most sensitive to changes in contrast. The N1 response is most sensitive to changes in contrast at high contrast levels, while the P1 response amplitude rises most at low-moderate contrasts, and then saturates at higher contrast levels. However, the age-related reduction in amplitude was limited to the 6 c/deg stimuli, making a definitive link of P1 amplitude changes to low spatial frequency sensitive magnocellular mechanisms rather difficult.

The contrast thresholds of the young and older observers were not significantly different, which excludes age-related differences in contrast sensitivity as a probable cause for the PREP amplitude differences found in the

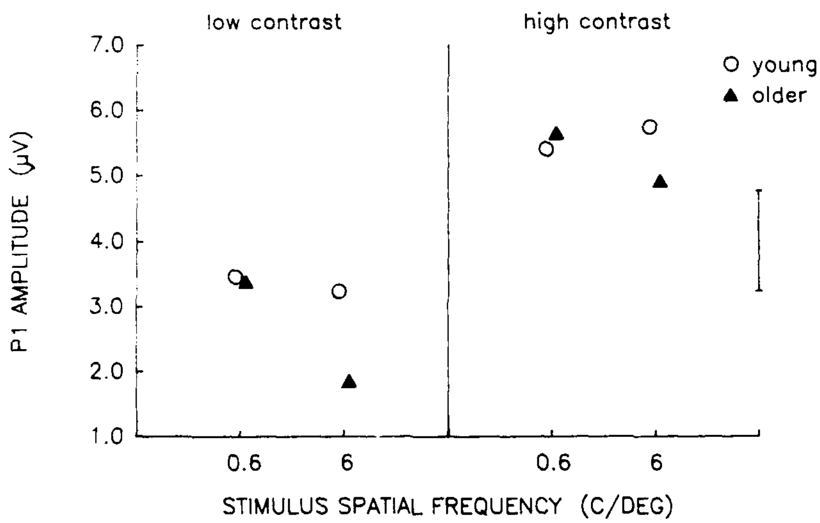

Fig. 3. Mean P1 amplitudes plotted as a function of stimulus spatial frequency and contrast level for young and older observers. Young subjects' data represented by (○), older subjects' data by (▲). The standard error for the means is shown at the right and is 1.53 μV.

present study. We did not employ a luminance-matched stimulus surround in our display, and thus the possibility exists that flicker at the edge of our display contributed to our findings. However, our results demonstrate-age-related amplitude differences only for high spatial frequency stimuli making it doubtful that flicker contamination was a significant factor in our results. A study designed to examine age-related PREP changes with and without stimulus surrounds would directly address this issue.

Perhaps of greater relevance to the present study are data which indicate that young and older observers have virtually equivalent suprathreshold contrast perception (Tulunay-Keesey *et al.*, 1988). To account for the presence of equivalent suprathreshold contrast perception in the face of age-related reductions in contrast sensitivity at higher flicker rates, Tulunay-Keesey *et al.* (1988) discuss the concept of suprathreshold compensation, which preserves high contrast vision regardless of low contrast visual change resulting from natural aging or disease conditions. If the age-related differences in N1 and P1 amplitudes reported in this paper do represent changes in visual system output with age, then some similar compensatory property must exist to normalize perceived contrast. It might be important in future studies to compare evoked potentials and psychophysical measures in the same observers in order to make a more valid comparison of these measures.

The present study serves to underscore the importance of utilizing stimuli for evoked potential studies which selectively stimulate hypothesized neural subsystems and thus permit accurate characterization of evoked potential components as a function of stimulus parameters. Sinusoidal gratings presented at low and high contrast levels revealed the presence of previously undetected age-related differences in PREP component amplitudes. The measurement of N1 and P1 PREP components under a variety of contrast and spatial frequency conditions may prove useful in the clinical application of the PREP for the early detection of disease conditions as well.

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REFERENCES

Allison T., Wood C. C. and Goff W. R. (1983) Brain stem auditory, pattern-reversal visual, and short latency somatosensory evoked potentials: latencies in relation to age, sex, and brain and body size. *Electroenceph. clin. Neurophysiol.* **55**, 619–636.

Allison T., Hume A. L., Wood C. C. and Goff W. R. (1984) Developmental and aging changes in somatosensory, auditory and visual evoked potentials. *Electroenceph. clin. Neurophysiol.* **58**, 14–24.

Bobak P., Bodis-Wollner I., Guillory S. and Anderson R. (1989) Aging differentially delays visual evoked potentials to checks and gratings. *Clin. Vision Sci.* **4**, 269–274.

Celesia G. G. and Daly R. F. (1977) Effects of aging on visual evoked responses. *Archs Neurol.* **34**, 403–407.

Celesia G. G., Kaufman D. and Cone S. (1987) Effects of age and sex on pattern electroretinograms and visual evoked potentials. *Electroenceph. clin. Neurophysiol.* **68**, 161–171.

Dreher B., Fukada Y. and Rodieck R. W. (1976) Identification, classification and anatomical segregation of cells with X-like and Y-like properties in the lateral geniculate nucleus of old-world primates. *J. Physiol., Lond.* **258**, 433–452.

Ginsburg A. P. and Cannon M. W. (1983) Comparison of three methods for rapid determination of threshold contrast sensitivity. *Invest. Ophthal. visual Sci.* **24**, 798–802.

Kaplan E. and Shapley R. M. (1982) X and Y cells in the lateral geniculate nucleus of macaque monkeys. *J. Physiol., Lond.* **330**, 125–143.

Kaplan E. and Shapley R. M. (1986) The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. *Proc. natl Acad. Sci. U.S.A.* **83**, 2755–2757.

La March J. A., Dobson W. R. Cohn N. B. and Dustman R. E. (1986) Amplitudes of visually evoked potentials to patterned stimuli: age and sex comparisons. *Electroenceph. clin. Neurophysiol.* **65**, 81–85.

Owsley C., Sekuler R. and Siemsen D. (1983) Contrast sensitivity throughout adulthood. *Vision Res.* **23**, 689–699.

Previc F. R. (1988) The neurophysiological significance of the N1 and P1 components of the visual evoked potential. *Clin. Vision Sci.* **3**, 195–202.

Shaw N. A. (1984) Changes in the cortical components of the visual evoked potential with age in man. *Aust. J. exp. Biol. med. Sci.* **62**, 771–778.

Shaw N. A. and Cant B. R. (1980) Age-dependent changes in the latency of the pattern visual evoked potential. *Electroenceph. clin. Neurophysiol.* **48**, 237–241.

Sloane M. E., Owsley C. and Alvarez S. (1988) Aging, senile miosis and spatial contrast sensitivity at low luminance. *Vision Res.* **28**, 1235–1246.

Snyder E. W., Dustman R. E. and Shearer D. E. (1981) Pattern reversal evoked potential amplitudes: life span changes. *Electroenceph. clin. Neurophysiol.* **52**, 429–434.

Sokol S., Moskowitz A. and Towle V. L. (1981) Age-dependent changes in the latency of the visual evoked potential: influence of check size. *Electroenceph. clin. Neurophysiol.* **51,** 559–562.

Stockard J. J., Hughes J. F. and Sharbrough F. W. (1979) Visual evoked potentials to electronic pattern reversal: latency variations with gender, age, and technical factors. *Am. J. EEG Technol.* **19,** 171–204.

Sturr J. F., Church K. L. and Taub H. A. (1988) Temporal summation functions for detection of sine-wave gratings in young and older adults. *Vision Res.* **28,** 1247–1253.

Tulunay-Keesey U., Ver Hoeve J. N. and Terkla-McGrane C. (1988) Threshold and suprathreshold spatiotemporal response throughout adulthood. *J. opt. Soc. Am A* **5,** 2191–2200.